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FILE COVERS 1907 - 17 Jan 2003 VOL 138 ISS 4

FILE LAST UPDATED: 16 Jan 2003 (20030116/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d stat que

L1 6958 SEA FILE=REGISTRY GSSE/SQSP
L2 51 SEA FILE=REGISTRY GHRELIN/BI
L3 2121 SEA FILE=REGISTRY OCTANOYL/BI
L4 2806 SEA FILE=HCAPLUS L1
L5 335 SEA FILE=HCAPLUS L2 OR GHRELIN?
L6 21439 SEA FILE=HCAPLUS L3 OR ?OCTANOYL?
L7 55 SEA FILE=HCAPLUS L4 AND L5
L8 17 SEA FILE=HCAPLUS L7 AND L6
L9 11 SEA FILE=HCAPLUS L7 AND ANTAGON?
L10 26 SEA FILE=HCAPLUS L8 OR L9

=> d ibib abs hitrn l10 1-26

L10 ANSWER 1 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:868955 HCAPLUS

DOCUMENT NUMBER: 137:367967

TITLE: Reproductive cancer diagnosis by detecting
ghrelin, exon 3-deleted form of preproghrelin
and GHS-R-1b expression and therapeutic methods
INVENTOR(S): Chopin, Lisa Kerstin; Jeffery, Penelope Lorrelle;
Herington, Adrian Charles
PATENT ASSIGNEE(S): Queensland University of Technology, Australia
SOURCE: PCT Int. Appl., 50 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT-NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2002090387 | A1 | 20021114 | WO 2002-AU582 | 20020510 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,

CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU,
TJ, TM

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH,
CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.:

AU 2001-4919 A 20010510
AU 2001-9567 A 20011217

- AB The invention relates to diagnosis and treatment of cancers of the reproductive system such as prostate cancer, breast cancer, ovarian cancer, cervical cancer and uterine cancer. The present inventors have discovered expression of **ghrelin**, growth hormone secretagogue receptor (GHS-R) 1a and GHS-R 1b by cancer cells and tissues of the reproductive system. Furthermore, expression of **ghrelin** and/or GHS-R 1b distinguishes cancer cells from normal cells, particularly in the case of prostate and breast cells and tissues. The present inventors have also identified a novel, exon 3-deleted form of preproghrelin, the expression of which distinguishes cancer cells and tissues from normal cells and tissues of the reproductive system. A method of detecting a cancer cell or tissue of the reproductive system uses detection of relatively increased levels of **ghrelin**, an exon 3-deleted form of preproghrelin and/or GHS-R 1b expression by cancer cells as compared to normal cells and tissues of the reproductive system. Also provided is an exon 3-deleted form of preproghrelin and antibodies thereto as well interventionist strategies that target **ghrelin** and/or GHS-Rs in treating cancers of the reproductive system such as prostate cancer and breast cancer, although without limitation thereto.
- IT 475211-58-6 475223-92-8D, subfragments are claimed
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(amino acid sequence; reproductive cancer diagnosis by detecting **ghrelin**, exon 3-deleted form of preproghrelin and GHS-R-1b expression and therapeutic methods)
- IT 475223-96-2, **Ghrelin**, prepro- (human)
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(amino acid sequence; reproductive cancer diagnosis by detecting **ghrelin**, exon 3-deleted form of preproghrelin and GHS-R-1b expression and therapeutic methods)
- IT 304853-26-7, **Ghrelin**
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); DGN (Diagnostic use); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(**ghrelin**; reproductive cancer diagnosis by detecting **ghrelin**, exon 3-deleted form of preproghrelin and GHS-R-1b expression and therapeutic methods)
- IT 475223-95-1D, subfragments are claimed
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); DGN (Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(nucleotide sequence; reproductive cancer diagnosis by detecting **ghrelin**, exon 3-deleted form of preproghrelin and GHS-R-1b expression and therapeutic methods)
- IT 322637-19-4, **Ghrelin**, prepro
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); DGN

(Diagnostic use); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses) (preproghrelin, exon 3-deleted form; reproductive cancer diagnosis by detecting **ghrelin**, exon 3-deleted form of preproghrelin and GHS-R-1b expression and therapeutic methods)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 2 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:594695 HCAPLUS

DOCUMENT NUMBER: 137:135505

TITLE: Remedies for undernutrition status

INVENTOR(S): Inui, Akio; Asakawa, Akihiro; Kaga, Toshihiro

PATENT ASSIGNEE(S): Chugai Seiyaku Kabushiki Kaisha, Japan

SOURCE: PCT Int. Appl., 50 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2002060472 | A1 | 20020808 | WO 2002-JP765 | 20020131 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |

PRIORITY APPLN. INFO.: JP 2001-24423 A 20010131

AB Remedies for diseases with undernutrition status such as inappetence, cachexia or malignant diseases and prostration caused by wt. loss in assocn. with infection or inflammatory diseases. These remedies contain as the active ingredient **ghrelin** or its analogs.

Ghrelin was intracerebroventricular (ICV) administered to mouse and its effect on feed intake was examd.

IT 304853-26-7, **Ghrelin**

RL: BSU (Biological study, unclassified); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

(**ghrelin** or related substances for treatment of undernutrition)

IT 313951-59-6

RL: PRP (Properties)

(unclaimed sequence; remedies for undernutrition status)

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 3 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:567376 HCAPLUS

DOCUMENT NUMBER: 137:304938

TITLE: Extent and direction of **ghrelin** transport across the blood-brain barrier is determined by its unique primary structure

AUTHOR(S): Banks, William A.; Tschop, Matthias; Robinson, Sandra

CORPORATE SOURCE: M.; Heiman, Mark L.
The Geriatric Research, Education, Veterans Affairs
Medical Center-St. Louis and the Division of
Geriatrics, Department of Internal Medicine, St. Louis
University School of Medicine, St. Louis, MO, USA

SOURCE: Journal of Pharmacology and Experimental Therapeutics
(2002), 302(2), 822-827
CODEN: JPETAB; ISSN: 0022-3565

PUBLISHER: American Society for Pharmacology and Experimental
Therapeutics

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The novel hormone **ghrelin** is a potent orexigen that may
counter-balance leptin. **Ghrelin** is the only secreted mol.
requiring post-translational acylation with octanoic acid to ensure
bioactivity. **Ghrelin**, predominantly derived from the stomach,
may target neuroendocrine networks within the central nervous system (CNS)
to regulate energy homeostasis. This would require **ghrelin** to
cross the blood-brain barrier (BBB). In mice, the authors examd. whether
ghrelin crosses the BBB and whether its lipophilic side chain is
involved in this process. The authors found that saturable systems
transported human **ghrelin** from brain-to-blood and from
blood-to-brain. Mouse **ghrelin**, differing from human
ghrelin by two amino acids, was a substrate for the
brain-to-blood, but not for the blood-to-brain transporter and so entered
the brain to a far lesser degree. Des-Octanoyl **ghrelin**
entered the brain by nonsaturable transmembrane diffusion and was
sequestered once within the CNS. In summary, the authors show that
ghrelin transport across the BBB is a complex, highly regulated
bidirectional process. The direction and extent of passage are detd. by
the primary structure of **ghrelin**, defining a new role for the
unique post-translational **octanoylation**.

IT 258279-04-8, Human **ghrelin** 258338-12-4,
Ghrelin (Rattus norvegicus) 304853-26-7, **Ghrelin**
307950-60-3
RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)
(extent and direction of **ghrelin** transport across blood-brain
barrier is detd. by its unique primary structure)

REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 4 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:450554 HCAPLUS

DOCUMENT NUMBER: 137:346579

TITLE: The GH-releasing effect of **ghrelin**, a
natural GH secretagogue, is only blunted by the
infusion of exogenous somatostatin in humans

AUTHOR(S): Di Vito, Lidia; Broglio, Fabio; Benso, Andrea;
Gottero, Cristina; Prodam, Flavia; Papotti, Mauro;
Muccioli, Giampiero; Dieguez, Carlos; Casanueva,
Felipe F.; Deghenghi, Romano; Ghigo, Ezio; Arvat,
Emanuela

CORPORATE SOURCE: Division of Endocrinology and Metabolism, Department
Internal Medicine, University of Turin, Italy

SOURCE: Clinical Endocrinology (Oxford, United Kingdom)
(2002), 56(5), 643-648
CODEN: CLECAP; ISSN: 0300-0664

PUBLISHER: Blackwell Science Ltd.

NW

DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Ghrelin**, a 28-amino-acid peptide purified from the stomach and showing a unique structure with an n-octanoyl ester at the serine 3 residue, is a natural ligand of the GH secretagogue (GHS) receptor (GHSR). **Ghrelin** strongly stimulates GH secretion in both animals and humans, showing a synergistic effect with GH-releasing hormone (GHRH) but no interaction with synthetic GHS. However, the activity of **ghrelin** as well as that of non-natural GHS is not fully specific for GH; **ghrelin** also induces a stimulatory effect on lactotroph and corticotroph secretion, at least in humans. To further clarify the mechanisms underlying the GH-releasing activity of this natural GHS, we studied the effects of somatostatin (SS, 2.0 $\mu\text{g/kg/h}$ from -30 to +90 min) on the endocrine responses to **ghrelin** (1.0 $\mu\text{g/kg}$ i.v. at 0 min) in seven normal young male volunteers [age (mean \pm SEM) 28.6 \pm 2.9 yr; body mass index (BMI) 22.1 \pm 0.8 kg/m^2]. In the same subjects, the effect of SS on the GH response to GHRH (1.0 $\mu\text{g/kg}$ i.v. at 0 min) was also studied. Blood samples were taken every 15 min from -30 up to +120 min. GH levels were assayed at each time point in all sessions; PRL, ACTH and cortisol levels were assayed after **ghrelin** administration alone and during SS infusion. The GH response to **ghrelin** (hAUC $_{0-120}$ 2695.0 \pm 492.6 $\mu\text{g min/l}$) was higher ($P < 0.01$) than that after GHRH (757.1 \pm 44.1 $\mu\text{g min/l}$). SS infusion almost abolished the GH response to GHRH (177.0 \pm 37.7 $\mu\text{g min/l}$, $P < 0.01$); the GH response to **ghrelin** was inhibited by SS (993.8 \pm 248.5 $\mu\text{g min/l}$, $P < 0.01$) but GH levels remained higher ($P < 0.05$) than with GHRH. **Ghrelin** induced significant increases in PRL, ACTH and cortisol levels and these responses were not modified by SS. **Ghrelin**, a natural GHS-R ligand, exerts a strong stimulatory effect on GH secretion in humans and this effect is only blunted by an exogenous somatostatin dose which almost abolishes the GH response to GHRH. The stimulatory effect of **ghrelin** on lactotroph and corticotroph secretion is refractory to exogenous somatostatin, indicating that these effects occur through pathways independent of somatostatinergic influence.

IT 258279-04-8, Human **ghrelin**

RL: BSU (Biological study, unclassified); BIOL (Biological study)
(effect of somatostatin on **ghrelin**-induced release of GH, prolactin, ACTH and cortisol)

REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 5 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2002:90068 HCAPLUS
DOCUMENT NUMBER: 136:129068
TITLE: **Ghrelin antagonist peptides**
INVENTOR(S): Deghenghi, Romano
PATENT ASSIGNEE(S): Zentaris A.-G., Germany
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2

DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2002008250 | A2 | 20020131 | WO 2001-EP7929 | 20010710 |
| WO 2002008250 | A3 | 20020822 | | |

W: AU, BG, BR, BY, CA, CN, CO, CZ, EE, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LT, LV, MK, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TR, UA, UZ, YU, ZA, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR

US 2002187938

A1

20021212

US 2001-902556

20010710

PRIORITY APPLN. INFO.:

US 2000-220178P P 20000724

my case

OTHER SOURCE(S):

MARPAT 136:129068

AB Novel peptides are disclosed having **antagonistic** properties to the Growth Hormone releasing peptide known as **Ghrelin**. The new peptides are useful in decreasing the circulating levels of Growth Hormone in a mammal and have therapeutic value. Peptide Gly-Ser-Ser(**Octanoyl**)-Phe, prepd. by solid phase synthesis, **antagonized** the effect of **ghrelin** by reducing growth hormone release in 10-day old rats.

IT 304853-26-7, **Ghrelin**

RL: ADV (Adverse effect, including toxicity); BSU (Biological study, unclassified); BIOL (Biological study)
(**ghrelin antagonist** peptides)

IT 342046-98-4P 342046-99-5P 392687-99-9P

RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(**ghrelin antagonist** peptides)

L10 ANSWER 6 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:902658 HCAPLUS

DOCUMENT NUMBER: 136:145365

TITLE: 1H NMR structural analysis of human **ghrelin** and its six truncated analogs

AUTHOR(S): Elipe, Maria Victoria Silva; Bednarek, Maria A.; Gao, Ying-Duo

CORPORATE SOURCE: Department of Drug Metabolism, Merck Research Laboratories, Rahway, NJ, USA

SOURCE: Biopolymers (2001), 59(7), 489-501

CODEN: BIPMAA; ISSN: 0006-3525

PUBLISHER: John Wiley & Sons, Inc.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Human **ghrelin**, the first recognized natural ligand of growth hormone secretagogue receptors (GHS-Rs), consists of 28 amino acids of which Ser 3 is modified by **n-octanoylation**. This new peptide hormone has been implicated not only in regulation of the GH secretion but also in regulation of food intake. The discovery of **ghrelin** opens up more opportunities to study the relationship of **ghrelin** with metabolic diseases. Until now, only mass spectrometry anal. has been reported on the structure of **ghrelin**. NMR anal. is a suitable way to study if any tertiary structure of unbound **ghrelin** is present in soln. NMR studies were carried out on human **ghrelin** and its five truncated analogs. The full-length **ghrelin** and its fragments exhibited random coil behavior in aq. soln. Addnl. studies were carried out on the shortest active segment of human **ghrelin**, which consists of the first five amino acids of the **ghrelin** sequence, to compare the spectral features with their counterparts in the full-length **ghrelin**. The NMR data showed behavior similar to **ghrelin** except for two addnl. nuclear Overhauser effects (NOEs) between the Phe 4 NH and the protons of the β -methylene of Ser 3. CD on human **ghrelin** and its short active analog in water were indicative of random coil peptides. Mol. modeling based on NMR data was

new

carried out to probe which structural features were similar to growth hormone-releasing peptide-6 (GHRP-6), a hexapeptide that binds to GHS-R releasing GH and stimulating food intake. Modeling suggested some similarities, but they were not of a nature to account for binding properties of these compds.

IT 258279-04-8, Human **ghrelin** 258279-04-8D, Human
ghrelin, truncated analogs 313951-59-6
313951-66-5 313951-71-2 313951-72-3
313951-73-4 313951-74-5

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)

(structural anal. of human **ghrelin** and truncated analogs in
relation to receptor binding)

REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 7 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:662512 HCAPLUS

DOCUMENT NUMBER: 135:366876

TITLE: Structure-Activity Relationship of **Ghrelin**:
Pharmacological Study of **Ghrelin** Peptides

AUTHOR(S): Matsumoto, Masaru; Hosoda, Hiroshi; Kitajima, Yasuo;
Morozumi, Naomi; Minamitake, Yoshiharu; Tanaka, Shoji;
Matsuo, Hisayuki; Kojima, Masayasu; Hayashi, Yujiro;
Kangawa, Kenji

CORPORATE SOURCE: Suntory Institute for Medicinal Research &
Development, Akaiwa, Chiyoda-machi, Ohra-gun, Gunma,
370-0503, Japan

SOURCE: Biochemical and Biophysical Research Communications
(2001), 287(1), 142-146

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Ghrelin**, a novel peptide purified from the stomach, is the
endogenous ligand of the growth hormone secretagogue receptor. The Ser3
residue of **ghrelin** is modified with a lipid n-octanoic acid, a
modification necessary for hormonal activity. To clarify the role of acyl
modification and to identify the active core of **ghrelin**, we
examd. the activities of partially digested **ghrelin** and
synthetic **ghrelin** derivs. The activities confirmed that the
N-terminal portion is the active core. Moreover, synthetic
ghrelin derivs. demonstrated that octanoic acid is not the only
modification of the Ser3 side chain to sustain the activity of
ghrelin; other acyl acid modifications maintained activity. Amino
acid replacement of Ser3 indicated that an L-configuration of the third
residue is crit. for **ghrelin** activity. In addn., more stable
ether or thioether bonds are capable of replacing the **octanoyl**
ester bond in **ghrelin**, advantageous for the generation of
pharmaceuticals with longer stability. (c) 2001 Academic Press.

IT 258279-04-8, Human **ghrelin** 258338-12-4, Rat
ghrelin 293735-04-3 304853-26-7,
Ghrelin 307950-60-3 321974-76-9
321974-78-1 321974-80-5 321974-82-7
321974-91-8 321974-93-0 321975-17-1
321975-27-3 342046-87-1 342046-88-2
342046-89-3 342046-90-6 342046-91-7
342046-96-2 342046-97-3 342046-98-4
342046-99-5 342047-04-5 374629-82-0

374629-83-1 374629-89-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structure-activity relationship pharmacol. study of **ghrelin** peptides)

REFERENCE COUNT: 10 THERE ARE 10 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 8 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:416023 HCAPLUS

DOCUMENT NUMBER: 135:175617

TITLE: Structural Similarity of **Ghrelin** Derivatives to Peptidyl Growth Hormone Secretagogues

AUTHOR(S): Matsumoto, Masaru; Kitajima, Yasuo; Iwanami, Tatsuya; Hayashi, Yujiro; Tanaka, Shoji; Minamitake, Yoshiharu; Hosoda, Hiroshi; Kojima, Masayasu; Matsuo, Hisayuki; Kangawa, Kenji

CORPORATE SOURCE: Suntory Institute for Medicinal Research & Development, Akaiwa, Chiyuoda-machi, Ohra-gun, Gunma, 370-0503, Japan

SOURCE: Biochemical and Biophysical Research Communications (2001), 284(3), 655-659

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Ghrelin** is a 28-amino acid residue endogenous growth hormone secretagogue. Intensive investigations revealed that the N-terminus tetrapeptide, having **octanoyl** group at Ser3, is the min. active core. In this study, we further explored the structure-function relationships of the active N-terminus portion of **ghrelin** using a Ca²⁺ mobilization assay. The smallest and most potent **ghrelin** deriv. we have found so far is 5-aminopentanoyl-Ser(Octyl)-Phe-Leu-aminoethylamide, showing comparable activity to the natural mol. In the process of modifying the active core, the **ghrelin**-derived short analogs emerged structurally close to peptidyl growth hormone secretagogues. The N-terminus modification suggested that Gly1-Ser2 unit works as a spacer, forming adequate distance between N.alpha.-amino group and n-**octanoyl** group. Replacement of 3rd and 4th amino acid residues to D-isomer suggested that the N-terminal dipeptide contributes to shape the biol. active geometry by effecting conformation of residues in positions 3 and 4. (c) 2001 Academic Press.

IT 258279-04-8, Human **ghrelin** 258338-12-4, **Ghrelin** (*Rattus norvegicus*) 313951-74-5

313951-75-6 321974-68-9 321974-72-5

321974-74-7 321974-84-9 321974-86-1

321974-88-3 321975-21-7 355424-19-0

355424-21-4 355424-24-7

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(structural similarity of **ghrelin** derivs. to peptidyl growth hormone secretagogues)

REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:311717 HCAPLUS

DOCUMENT NUMBER: 135:602

TITLE: Structure-activity relationships of **ghrelin**:

AUTHOR(S): endogenous growth hormone secretagogue
Matsumoto, Masaru; Kitajima, Yasuo; Iwanami, Tatsuya;
Morozumi, Naomi; Hayashi, Yujiro; Tanaka, Shoji;
Minamitake, Yoshiharu; Hosoda, Hiroshi; Kojima,
Masayasu; Matsuo, Hisayuki; Kangawa, Kenji

CORPORATE SOURCE: Institute for Medicinal R&D, Suntory Limited, Gunma,
370-0503, Japan

SOURCE: Peptide Science (2001), Volume Date 2000, 37th,
101-104
CODEN: PSCIFQ; ISSN: 1344-7661

PUBLISHER: Japanese Peptide Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Ghrelin**, an endogenous ligand for growth hormone
secretagogue-receptor (GHS-R), consists of 28 amino acid residues with
unique **octanoyl** modification at Ser3. **Ghrelin** derivs.
were systematically synthesized to investigate the roles of acyl group,
length of fatty acid, peptide length, etc. The assay using cells
expressing GHS-R demonstrated that N-terminus (1-4) with hydrophobicity at
the 3rd residue was essential to increase intracellular Ca²⁺, suggesting
that it is the active core structure. Structural similarity of the
derivs. to synthetic GHSs is also discussed.

IT 258279-04-8P, Human **ghrelin** 258338-12-4P, Rat
ghrelin 313951-74-5P 313951-75-6P
321974-68-9P 321974-72-5P 321974-76-9P
321974-78-1P 321974-80-5P 321974-82-7P
321974-84-9P 321974-86-1P 321974-88-3P
321974-91-8P 321974-93-0P 321975-17-1P
321975-27-3P 321975-29-5P 321975-31-9P
321975-33-1P 321975-35-3P 342046-87-1P
342046-88-2P 342046-89-3P 342046-90-6P
342046-91-7P 342046-93-9P 342046-95-1P
342046-96-2P 342046-97-3P 342046-98-4P
342046-99-5P 342047-04-5P

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP
(Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP
(Preparation); PROC (Process)
(structure-activity relationships of **ghrelin** in relation to
binding affinity of **ghrelin** derivs. to endogenous growth
hormone secretagogue receptor)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:308211 HCAPLUS

DOCUMENT NUMBER: 134:361621

TITLE: Binding of 125I-labeled **ghrelin** to membranes
from human hypothalamus and pituitary gland

AUTHOR(S): Muccioli, G.; Papotti, M.; Locatelli, V.; Ghigo, E.;
Deghenghi, R.

CORPORATE SOURCE: Division of Pharmacology, Department of Anatomy,
Pharmacology and Forensic Medicine, University of
Turin, Turin, 10125, Italy

SOURCE: Journal of Endocrinological Investigation (2001),
24(3), RC7-RC9
CODEN: JEIND7; ISSN: 0391-4097

PUBLISHER: Editrice Kurtis s.r.l.

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Ghrelin** has been proposed as a natural ligand of the GH secretagogue receptor(s) (GHS-R), which was an orphan receptor activated by synthetic peptidyl (hexarelin) and non-peptidyl (MK-0677) GHS to strongly release GH in animals and humans. Herein the authors studied: (1) the binding of 125I-labeled human **ghrelin** to membranes from human hypothalamus and pituitary gland; (2) the ability of human **ghrelin** (either **octanoylated** or **desoctanoylated**), as well as of some GHS and neuropeptides to compete with the radioligand. The satn. binding anal. showed, in both tissues, the existence of a single class of high-affinity binding sites with limited binding capacity. The Bmax (maximal no. of binding sites) values of **ghrelin** receptors in the hypothalamus were significantly greater than those detected in the pituitary, whereas the Kd (dissocon. const.) values in the two tissues were similar. 125I-**ghrelin** bound to hypothalamic membranes was displaced by **ghrelin**, hexarelin, MK-0677, various GHS **antagonists** (EP-80317, [D-Arg1-D-Phe5-D-Trp7,9-Leu11]-substance P) and some natural (cortistatin-14) and synthetic (vapreotide) SRIH-14 agonists. In contrast, no competition was seen in the presence of GHRH-44, SRIH-14 or **desoctanoylated ghrelin**, a **ghrelin** precursor that is devoid of GH-releasing properties. In conclusion, this preliminary study firstly demonstrates that **ghrelin** needs **octanoylation** to bind its hypothalamo-pituitary receptors. These receptors are the specific binding sites for GHS and their **antagonists**, as well as for SRIH analogs (vapreotide and cortistatin-14), but not for native SRIH.

IT 258279-04-8, Human **ghrelin** 304853-26-7, **Ghrelin**

RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(characterization of **ghrelin** binding to membranes from human hypothalamus and pituitary gland)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 11 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:284719 HCAPLUS

DOCUMENT NUMBER: 135:59298

TITLE: Identification, characterization, and biological activity of specific receptors for natural (**ghrelin**) and synthetic growth hormone secretagogues and analogs in human breast carcinomas and cell lines

AUTHOR(S): Cassoni, Paola; Papotti, Mauro; Ghe, Corrado; Catapano, Filomena; Sapino, Anna; Graziani, Andrea; Deghenghi, Romano; Reissmann, Thomas; Ghigo, Ezio; Muccioli, Giampiero

CORPORATE SOURCE: Departments of Biomedical Sciences and Oncology, University of Turin, Turin, 10126, Italy

SOURCE: Journal of Clinical Endocrinology and Metabolism (2001), 86(4), 1738-1745

CODEN: JCEMAZ; ISSN: 0021-972X

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The family of GH secretagogues (GHS) includes synthetic peptidyl (hexarelin) and nonpeptidyl (MK-0677) mols. possessing specific receptors in the pituitary and central nervous system as well as in peripheral tissues, including the heart and some endocrine organs. A gastric-derived peptide, named **ghrelin**, has recently been proposed as the

natural ligand of the GHS receptors (GHS-Rs). The presence of specific GHS-Rs has now been investigated in nontumoral and neoplastic human breast tissue using a radioiodinated peptidyl GHS ([125I]-Tyr-Ala-hexarelin) as ligand. Specific binding sites for GHS were detected in membranes from several types of breast carcinomas, whereas a negligible binding was found in fibroadenomas and mammary parenchyma. The highest binding activity was found in well-differentiated (G1) invasive breast carcinomas and was progressively reduced in moderately (G2) to poorly (G3) differentiated tumors. [125I]-Tyr-Ala-hexarelin bound to tumor membranes was displaced by different unlabeled GHS such as hexarelin, Tyr-Ala-hexarelin, human ghrelin, and MK-0677 as well as by desoctanoyl-ghrelin and hexarelin deriv. EP-80317, which are devoid of GH-releasing properties in vivo. In contrast, no competition was seen between radiolabeled Tyr-Ala-hexarelin and some peptides (CRF and insulin-like growth factor I) structurally and functionally unrelated to hexarelin or when GHRH and SRIF were tested in the displacement studies. The presence of specific GHS binding sites was also demonstrated in three different human breast carcinoma cell lines (MCF7, T47D, and MDA-MB231), in which, surprisingly, no mRNA for GHS-R1a was demonstrated by RT-PCR. In these cell lines, ghrelin (as well as hexarelin, MK-0677, EP-80317, and even desoctanoyl ghrelin) caused a significant inhibition of cell proliferation at concns. close to their binding affinity. In conclusion, this study provides the first demonstration of specific GHS binding sites, other than GHS-R1, in breast cancer. These receptors probably mediate growth inhibitory effects on breast carcinoma cells in vitro.

IT 258279-04-8, Human ghrelin

RL: BOC (Biological occurrence); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); OCCU (Occurrence); PROC (Process)

(identification, characterization, and biol. activity of specific receptors for natural (ghrelin) and synthetic growth hormone secretagogues and analogs in human breast carcinomas and cell lines)

REFERENCE COUNT: 35 THERE ARE 35 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 12 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:211447 HCAPLUS

DOCUMENT NUMBER: 134:247416

TITLE: Endocrine activities of ghrelin, a natural growth hormone secretagogue (GHS), in humans: comparison and interactions with hexarelin, a nonnatural peptidyl GHS, and GH-releasing hormone

AUTHOR(S): Arvat, Emanuela; Maccario, Mauro; Di Vito, Lidia; Broglio, Fabio; Benso, Andrea; Gottero, Cristina; Papotti, Mauro; Muccioli, Giampiero; Dieguez, Carlos; Casanueva, Felipe F.; Deghenghi, Romano; Camanni, Franco; Ghigo, Ezio

CORPORATE SOURCE: Division of Endocrinology and Metabolism, Department of Internal Medicine, University of Turin, Turin, 10126, Italy

SOURCE: Journal of Clinical Endocrinology and Metabolism (2001), 86(3), 1169-1174

CODEN: JCEMAZ; ISSN: 0021-972X

PUBLISHER: Endocrine Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB An endogenous ligand for the GH secretagogue-receptor (GHS-receptor) has recently been isolated, from both the rat and the human stomach, and named

ghrelin. It is a 28-amino-acid peptide showing a unique structure with an n-octanoyl ester at its third serine residue, which is essential for its potent stimulatory activity on somatotroph secretion. In fact, it has been demonstrated that **ghrelin** specifically stimulates GH secretion from both rat pituitary cells in culture and rats in vivo. The aim of the present study was to test the GH-releasing activity of **ghrelin** in humans and to compare it with that of GHRH and hexarelin (HEX), a nonnatural peptidyl GHS, which possesses strong GH-releasing activity but also significantly stimulates PRL, ACTH, and cortisol secretion. To clarify the mechanisms of action underlying the GH-releasing activity of **ghrelin** in humans, its interaction with GHRH and HEX was also studied. Seven normal young volunteers (7 men; 24-32 yr old; body mass index, 20-24 kg/m²) were studied. All subjects underwent the administration of **ghrelin**, HEX, and GHRH-29 (1.0 .mu.g/kg i.v. at 0 min) as well as placebo (2 mL isotonic saline i.v. at 0 min). Six subjects also underwent the combined administration of **ghrelin** and GHRH or HEX. Blood samples were taken every 15 min from -15 up to +180 min. GH levels were assayed at each time point in all sessions; PRL, ACTH, cortisol, and aldosterone levels were also assayed after administration of **ghrelin** and/or HEX. **Ghrelin** administration induced a prompt and marked increase in circulating GH levels (Cmax, mean, 92.1 .mu.g/L; area under the curve, 1894.9 .mu.g/L.cntdot.h). The GH response to **ghrelin** was clearly higher than the one recorded after GHRH (26.7 .mu.g/L; 619.6 .mu.g/L.cntdot.h) and even significantly higher than after HEX (68.4 .mu.g/L; 1546.9 .mu.g/L.cntdot.h). **Ghrelin** administration also induced an increase in PRL, ACTH, and cortisol levels; these responses were higher than those elicited by HEX. A significant increase in aldosterone levels was recorded after **ghrelin** but not after HEX. The endocrine responses to **ghrelin** were not modified by the coadministration of HEX. On the other hand, the coadministration of **ghrelin** and GHRH had a real synergistic effect on GH secretion (133.6 .mu.g/L; 3374.3 .mu.g/L.cntdot.h). In conclusion, **ghrelin**, a natural ligand of GHS-receptor, exerts a strong stimulatory effect on GH secretion in humans, releasing more GH than GHRH and even more than a non-natural GHS such as HEX. **Ghrelin**, as well as HEX, also stimulates lactotroph and corticotroph secretion. **Ghrelin** shows no interaction with HEX, whereas it has a synergistic effect with GHRH on GH secretion. Thus, **ghrelin** is a new hormone playing a major role in the control of somatotroph secretion in humans, and its effects are imitated by nonnatural GHS.

IT 258279-04-8, Human **ghrelin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**ghrelin** stimulation of corticosteroids and pituitary hormones in humans and comparative and interactive effects with hexarelin and GH-releasing hormone)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 13 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:152059 HCAPLUS

DOCUMENT NUMBER: 134:247409

TITLE: Cortistatin, but not somatostatin, binds to growth hormone secretagogue (GHS) receptors of human pituitary gland

AUTHOR(S): Deghenghi, R.; Papotti, M.; Ghigo, E.; Muccioli, G.

CORPORATE SOURCE:uropeptides, Argenteuil, 95108, Fr.

SOURCE: Journal of Endocrinological Investigation (2001),

24(1), RC1-RC3

CODEN: JEIND7; ISSN: 0391-4097

PUBLISHER:

Editrice Kurtis s.r.l.

DOCUMENT TYPE:

Journal

LANGUAGE:

English

AB **Antagonism** between GH secretagogues (GHS) and somatostatin (SRIH) has been postulated and demonstrated, but SRIH does not bind to GHS receptors (GHS-R) and potent synthetic peptidyl GHS (GHRP6, hexarelin) do not displace radiolabeled SRIH from its receptors. However, non-natural SRIH octapeptide agonists (mainly lanreotide and vapreotide) displace 125I-Tyr-Ala-hexarelin from pituitary binding sites suggesting that an endogenous factor related to SRIH might exist and interact with GHS-R. The authors' aims were to investigate the ability of different SRIH-like peptides such as various SRIH fragments (SRIH 3-14, SRIH 7-14, SRIH 3-10, SRIH 7-10, SRIH 2-9) and a natural neuropeptide that shows a high structural homol. with SRIH such as cortistatin-14 (CST) to compete with 125I-Tyr-Ala-hexarelin for human pituitary binding sites and to compare their binding affinity with that of hexarelin and **ghrelin**, a gastric-derived peptidyl GHS that has been proposed as a natural ligand of GHS-R. While the binding of 125I-Tyr-Ala-hexarelin to pituitary membranes was completely displaced by unlabeled hexarelin, **ghrelin** and CST, none of the SRIH fragments tested inhibited this binding. **Ghrelin** and CST exhibited a similar affinity (4.6-5.4 .times. 10⁻⁷ mol/l) for the binding while hexarelin was more effective by about four orders of magnitude in displacing 125I-Tyr-Ala-hexarelin. The authors' data demonstrate for the first time that cortistatin, a natural peptide related to SRIH, binds to GHS-R and suggest that this factor may play a role in modulating the activity of these receptors.

IT **258279-04-8, Human ghrelin**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(cortistatin but not somatostatin binds to growth hormone secretagogue receptors of human pituitary gland)

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 14 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:151118 HCAPLUS

DOCUMENT NUMBER: 134:202794

TITLE: In vivo and in vitro effects of **ghrelin** /motilin-related peptide on growth hormone secretion in the rat

AUTHOR(S): Tolle, Virginie; Zizzari, Philippe; Tomasetto, Catherine; Rio, Marie-Christine; Epelbaum, Jacques; Bluet-Pajot, Marie-Therese

CORPORATE SOURCE: U159 INSERM, Paris, Fr.

SOURCE: Neuroendocrinology (2001), 73(1), 54-61

CODEN: NUNDAJ; ISSN: 0028-3835

PUBLISHER: S. Karger AG

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Ghrelin** (Ghr), a 28 amino acid gastric peptide with an n-octanoylation on Ser 3, has recently been identified as an endogenous ligand of the growth hormone secretagogue (GHS) receptor. A cDNA was also isolated from a mouse stomach library encoding a protein named prepromotilin-related peptide (ppMTLRP) which shares sequence similarities with prepromotilin. Mouse and rat ppMTLRP sequences (rGhr) are identical and show 89% identity with human **ghrelin** (hGhr).

By analogy with promotilin, cleavage of proMTLRP into an 18 amino acid endogenous processed peptide can be assumed on the basis of a conserved dibasic motif in position 9-10 of its sequence. In the present work, the authors compared the GH-releasing activity of rGhr28/MTLRP and of hGhr28/MTRLRP with that of a shorter form of the peptide, hGhr18. A short peptide devoid of Ser 3 n-octanoylation hGhr18[-] was also tested. Addn. of rGhr28, hGhr28 and hGhr18 stimulated GH release to the same extent from superfused pituitaries. The effect was dose dependent in a 10⁻⁸ to 10⁻⁶ M concn. range. In contrast, hGhr 18[-] was inactive. In freely moving animals, both rGhr28 and hGhr28 (10 .mu.g, i.v.) stimulated GH release, whereas the same dose of hGhr18 or of hGhr18[-] was ineffective. After rGhr28, GH plasma levels increased as early as 5 min after injection and returned to basal values within 40-60 min. Expressed as percent stimulation, administration of rGhr28 was equally effective when injected during troughs or peaks of GH. Plasma concns. of prolactin, ACTH and leptin were not modified. Spontaneous GH secretory episodes were no longer obsd. within 3 h of rGhr28 treatment, but repeated administration of the secretagogue at 3- to 4-h intervals resulted in a similar GH response. Activation of somatostatin (SRIH) release by ether stress did not blunt the GH response to rGhr28. This suggests that the secretagogue acts in part by inhibiting endogenous SRIH, as further substantiated by the ability of rGhr28 (10⁻⁶ M), to decrease the amplitude of 25 mM K+-induced SRIH release from perfused hypothalami. In conclusion, (1) n-octanoylation of Ghre and the shorter form hGhr18 is essential for the direct pituitary GH-releasing effect of this new family of endogenous GHSs; (2) only the longer forms are active in vivo and (3) inhibition of SRIH release appears involved in the mechanism of Ghr action.

IT 213815-74-8 258279-04-8, Human ghrelin

258338-12-4, Rat ghrelin 328943-80-2

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(ghrelin effects on growth hormone secretion in relation to structure)

IT 304853-26-7, Ghrelin

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study)
(mol. forms; ghrelin effects on growth hormone secretion in relation to structure)

REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 15 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:107297 HCAPLUS

DOCUMENT NUMBER: 134:275978

TITLE: Ghrelin, an endogenous growth hormone secretagogue, is a novel orexigenic peptide that antagonizes leptin action through the activation of hypothalamic neuropeptide Y/Y1 receptor pathway

AUTHOR(S): Shintani, Mitsuyo; Ogawa, Yoshihiro; Ebihara, Ken; Aizawa-Abe, Megumi; Miyanaga, Fumiko; Takaya, Kazuhiko; Hayashi, Tatsuya; Inoue, Gen; Hosoda, Kiminori; Kojima, Masayasu; Kangawa, Kenji; Nakao, Kazuwa

CORPORATE SOURCE: Department of Medicine and Clinical Science, Kyoto University Graduate School of Medicine, Kyoto, 606-8507, Japan

SOURCE: Diabetes (2001), 50(2), 227-232

PUBLISHER:

CODEN: DIAEAZ; ISSN: 0012-1797

DOCUMENT TYPE:

American Diabetes Association

LANGUAGE:

Journal

English

AB **Ghrelin**, an endogenous ligand for growth hormone secretagogue (GHS) receptor originally isolated from the stomach, occurs in the hypothalamic arcuate nucleus and may play a role in energy homeostasis. Synthetic GHSs have activated the hypothalamic arcuate neurons contg. neuropeptide Y (NPY), suggesting the involvement of NPY in some of **ghrelin** actions. This study was designed to elucidate the role of **ghrelin** in the regulation of food intake. A single intracerebroventricular (ICV) injection of **ghrelin** (5-5000 ng/rat) caused a significant and dose-related increase in cumulative food intake in rats. **Ghrelin** (500 ng/rat) was also effective in growth hormone-deficient spontaneous dwarf rats. Hypothalamic NPY mRNA expression was increased in rats that received a single ICV injection of **ghrelin** (500 ng/rat) (.apprx.160% of that in vehicle-treated groups). The **ghrelin**'s orexigenic effect was abolished dose-dependently by ICV co-injection of NPY Y1 receptor **antagonist** (10-30 .mu.g/rat). The leptin-induced inhibition of food intake was reversed by ICV co-injection of **ghrelin** in a dose-dependent manner (5-500 ng/rat). Leptin reduced hypothalamic NPY mRNA expression by 35%, which was abolished by ICV co-injection of **ghrelin** (500 ng/rat). This study provides evidence that **ghrelin** is an orexigenic peptide that **antagonizes** leptin action through the activation of hypothalamic NPY/Y1 receptor pathway.

IT 258279-04-8, Human **ghrelin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**ghrelin** as orexigenic peptide that **antagonizes**

leptin action through activation of hypothalamic neuropeptide Y1 receptor pathway in rats)

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 16 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:78416 HCAPLUS

DOCUMENT NUMBER: 134:142304

TITLE: Novel **ghrelins**, their encoding DNA sequences, and their use as therapeutics

INVENTOR(S): Kangawa, Kenji; Kojima, Masayasu; Hosoda, Hiroshi; Matsuo, Hisayuki; Minamitake, Yoshiharu

PATENT ASSIGNEE(S): Japan

SOURCE: PCT Int. Appl., 210 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: Japanese

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|--|----------|-----------------|----------|
| WO 2001007475 | A1 | 20010201 | WO 2000-JP4907 | 20000724 |
| W: | AE, AG, AL, AM, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CN, CR, CU, CZ, DM, DZ, EE, GD, GE, HR, HU, ID, IL, IN, IS, JP, KG, KR, KZ, LC, LK, LR, LT, LV, MA, MD, MG, MK, MN, MX, NO, NZ, PL, RO, RU, SG, SI, SK, TJ, TM, TR, TT, UA, US, UZ, VN, YU, ZA, ZM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, | | | |

DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
BR 2000012688 A 20020416 BR 2000-12688 20000724
EP 1197496 A1 20020417 EP 2000-946453 20000724

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

JP 1999-210002 A 19990723
JP 1999-338841 A 19991129
JP 2000-126623 A 20000426
WO 2000-JP4907 W 20000724

- AB Novel **ghrelins**, the natural ligands for growth hormone (GH) secretagogue receptors, and their derivs. that have .gtoreq.1 amino acid substituted with a modified amino acid or non-amino acid compd. are prepd. and used as a therapeutic for inducing the secretion of growth hormone. **Ghrelins** are also able to increase the intracellular concn. of calcium ions. An 117-amino acid **ghrelin** isolated from the stomach of rats contains a serine deriv. (3rd residue) that is modified with n-octanoyl (C8:0) fatty acid. **Ghrelins** and their encoding cDNA sequences isolated from human and other animals are also shown. The structural-activity relationship of chem. synthesized **ghrelin** derivs. of human or rats were also described. Claimed are methods for recombinant prepn. of **ghrelins**, antibodies to **ghrelins**, methods for immunoassay of **ghrelins**, and use of **ghrelins** for treating the diseases assocd. with growth hormone deficiency.
- IT 213825-66-2D, O-fatty acyl derivs. 258259-89-1D, O-fatty acyl derivs. 293339-41-0D, O-fatty acyl derivs. 322483-09-0D, O-fatty acyl derivs. 322483-12-5 322483-13-6 322483-15-8, **Ghrelin** (cattle prepro fragment) 322483-17-0, **Ghrelin** (Anguilla japonica prepro) 322483-18-1, **Ghrelin** (Xenopus laevis prepro) 322483-19-2 322483-20-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(amino acid sequence; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 321974-56-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(core region of Anguilla japonica growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 321974-66-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(core region of Canis familiaris growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 321974-54-3
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(core region of Gallus domesticus growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 321974-62-3 321974-64-5
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)

- (core region of *Oncorhynchus mykiss* growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 321974-52-1
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (core region of cattle growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 321974-36-1D, O-fatty acyl derivs. 321974-40-7D, O-fatty acyl derivs. 321974-42-9D, O-fatty acyl derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (core region of growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 313951-59-6D, O-fatty acyl derivs. 321974-46-3D, O-fatty acyl derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (core region of human growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 307950-60-3D, O-fatty acyl derivs. 321974-44-1D, O-fatty acyl derivs.
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (core region of rat growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 321974-48-5 321974-50-9
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (core region of swine growth hormone secretagogue; novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 313951-75-6P 321974-68-9P 321974-70-3P
321974-72-5P 321974-74-7P 321974-76-9P
321974-78-1P 321974-80-5P 321974-82-7P
321974-84-9P 321974-86-1P 321974-88-3P
321974-91-8P 321974-93-0P 321974-95-2P
321974-97-4P 321974-99-6P 321975-17-1P
321975-19-3P 321975-21-7P 321975-23-9P
321975-27-3P 321975-29-5P 321975-31-9P
321975-33-1P 321975-35-3P 321975-37-5P
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
- (novel **ghrelins**, encoding DNA sequences, and use as therapeutics)
- IT 252925-13-6 252925-14-7, DNA (human **ghrelin** cDNA plus flanks) 308789-38-0 322483-10-3
322483-11-4 322483-14-7 322483-16-9, DNA (cattle **ghrelin** cDNA fragment) 322483-21-6
322483-22-7
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
- (nucleotide sequence; novel **ghrelins**, encoding DNA sequences,

and use as therapeutics)

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 17 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:59050 HCAPLUS

DOCUMENT NUMBER: 134:126261

TITLE: A role for **ghrelin** in the central regulation of feeding

AUTHOR(S): Nakazato, Masamitsu; Murakami, Noboru; Date, Yukari; Kojima, Masayasu; Matsuo, Hisayukil; Kangawa, Kenji; Matsukura, Shigeru

CORPORATE SOURCE: Third Department of Internal Medicine, Miyazaki

SOURCE: Medical College, Kiyotake, Miyazaki, 889-1692, Japan Nature (London) (2001), 409(6817), 194-198

CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Nature Publishing Group

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Ghrelin** is an acylated peptide that stimulates the release of growth hormone from the pituitary. **Ghrelin**-producing neurons are located in the hypothalamus, whereas **ghrelin** receptors are expressed in various regions of the brain, which is indicative of central-and as yet. undefined-physiol. functions. Here **ghrelin** is involved in the hypothalamic regulation of energy homeostasis. Intracerebroventricular injections of **ghrelin** strongly stimulated feeding in rats and increased body wt. gain. **Ghrelin** also increased feeding in rats that are genetically deficient in growth hormone. Anti-**ghrelin** IgG robustly suppressed feeding. After intracerebroventricular **ghrelin** administration, Fos protein, a marker of neuronal activation, was found in regions of primary importance in the regulation of feeding, including neuropeptide Y (NPY) neurons and agouti-related protein (AGRP) neurons. Antibodies and antagonists of NPY and AGRP abolished **ghrelin**-induced feeding. **Ghrelin** augmented NPY gene expression and blocked leptin-induced feeding redn., implying that there is a competitive interaction between **ghrelin** and leptin in feeding regulation. The authors conclude that **ghrelin** is a physiol. mediator of feeding, and probably has a function in growth regulation by stimulating feeding and release of growth hormone. new

IT 304853-26-7, **Ghrelin**

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)

(**ghrelin** role in central regulation of feeding in rat in relation to role of neuropeptide Y, leptin and agouti related protein)

IT 258338-12-4, Rat **ghrelin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)

(**ghrelin** role in central regulation of feeding in rat in relation to role of neuropeptide Y, leptin and agouti related protein)

REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 18 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:28272 HCAPLUS

DOCUMENT NUMBER: 134:110732

TITLE: **Ghrelin** and des-acyl **ghrelin**: two major forms of rat **ghrelin** peptide in I have

Searched by M. Smith

18, 20

AUTHOR(S): gastrointestinal tissue
Hosoda, Hiroshi; Kojima, Masayasu; Matsuo, Hisayuki;
Kangawa, Kenji
CORPORATE SOURCE: Department of Biochemistry, National Cardiovascular
Center Research Institute, Suita, Osaka, 565-8565,
Japan
SOURCE: Biochemical and Biophysical Research Communications
(2000), 279(3), 909-913
CODEN: BBRCA9; ISSN: 0006-291X
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB **Ghrelin**, a novel peptide purified from stomach, is the endogenous ligand for the growth hormone secretagogue receptor and has potent growth hormone-releasing activity. The Ser 3 residue of **ghrelin** is modified by n-octanoic acid, a modification necessary for hormonal activity. The authors established two **ghrelin**-specific RIAs; one recognizes the **octanoyl**-modified portion and another the C-terminal portion of **ghrelin**. Using these RIA systems, the authors found that two major mol. forms exist-**ghrelin** and des-n-octanoyl **ghrelin**. While **ghrelin** activates growth-hormone secretagogue (GHS) receptor-expressing cells, the nonmodified des-n-octanoyl form of **ghrelin**, designated as des-acyl **ghrelin**, does not. In addn. to these findings, the authors' RIA systems also revealed high concns. of **ghrelin** in the stomach and small intestine. (c) 2000 Academic Press.

IT 304853-26-7, **Ghrelin** 304853-26-7D,
Ghrelin, des-n-octanoyl derivs.

RL: ANT (Analyte); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); ANST (Analytical study); BIOL (Biological study); PROC (Process)
(**ghrelin** and des-acyl **ghrelin** in relation to two major forms of rat **ghrelin** peptide in gastrointestinal tissue)

IT 258338-12-4, Rat **ghrelin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**ghrelin** and des-acyl **ghrelin** in relation to two major forms of rat **ghrelin** peptide in gastrointestinal tissue)

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 19 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:12624 HCAPLUS

DOCUMENT NUMBER: 134:81777

TITLE: Protein and cDNA sequences of novel human protein SGIP and therapeutic uses thereof

INVENTOR(S): Sheppard, Paul O.; Jaspers, Stephen R.; Deisher, Theresa A.; Bishop, Paul D.

PATENT ASSIGNEE(S): Zymogenetics, Inc., USA

SOURCE: PCT Int. Appl., 61 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.

KIND DATE

APPLICATION NO. DATE

WO 2001000830 A1 20010104 WO 2000-US18306 20000630
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR,
CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU,
ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU,
LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE,
SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,
DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ,
CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
EP 1190059 A1 20020327 EP 2000-945123 20000630
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO

PRIORITY APPLN. INFO.:

US 1999-345157 A 19990630

WO 2000-US18306 W 20000630

AB The present invention provides protein and cDNA sequences of a novel human protein SGIP which have homol. to motilin. Tissue distribution of the mRNA for the novel polypeptide fragment is specific to the stomach, small intestine and pancreas. Binding of the peptide fragment has been shown in kidney and small intestine. The SGIP gene resides on human chromosome 3 at 3p26.1. The present invention further includes agonists, **antagonists**, variants, antibodies and host cells expressing the cDNA encoding the novel SGIP peptide. *

IT 316363-83-4P

RL: BAC (Biological activity or effector, except adverse); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)

(amino acid sequence; protein and cDNA sequences of novel human protein SGIP and therapeutic uses thereof)

IT 213825-66-2

RL: PRP (Properties)

(unclaimed protein sequence; protein and cDNA sequences of novel human protein SGIP and therapeutic uses thereof)

REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 20 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:758603 HCAPLUS

DOCUMENT NUMBER: 134:51509

TITLE: Structure-Function Studies on the New Growth

Hormone-Releasing Peptide, **Ghrelin**: Minimal Sequence of **Ghrelin** Necessary for Activation of Growth Hormone Secretagogue Receptor 1a

AUTHOR(S): Bednarek, Maria A.; Feighner, Scott D.; Pong, Sheng-Shung; McKee, Karen Kulju; Hreniuk, Donna L.; Silva, Maria V.; Warren, Vivien A.; Howard, Andrew D.; Van der Ploeg, Lex H. Y.; Heck, James V.

CORPORATE SOURCE: Departments of Medicinal Chemistry Metabolic Disorders Drug Metabolism and Membrane Biochemistry and Biophysics, Merck Research Laboratories, Rahway, NJ, 07065, USA

SOURCE: Journal of Medicinal Chemistry (2000), 43(23), 4370-4376

CODEN: JMCMAR; ISSN: 0022-2623

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

AB The recently discovered growth hormone secretagogue, **ghrelin**, is a potent agonist at the human growth hormone secretagogue receptor 1a (hGHSR1a). To elucidate structural features of this peptide necessary for efficient binding to and activation of the receptor, several analogs of **ghrelin** with various aliph. or arom. groups in the side chain of residue 3, and several short peptides derived from **ghrelin**, were prepd. and tested in a binding assay and in an assay measuring intracellular calcium elevation in HEK-293 cells expressing hGHSR1a. Bulky hydrophobic groups in the side chain of residue 3 turned out to be essential for max. agonist activity. Also, short peptides encompassing the first 4 or 5 residues of **ghrelin** were found to functionally activate hGHSR1a about as efficiently as the full-length **ghrelin**. Thus, the entire sequence of **ghrelin** is not necessary for activity: the Gly-Ser-Ser(n-octanoyl)-Phe segment appears to constitute the "active core" required for agonist potency at hGHSR1a. *too much*

IT 258279-04-8, Ghrelin (human) 313951-54-1

313951-55-2 313951-56-3 313951-57-4

313951-58-5 313951-59-6 313951-60-9

313951-61-0 313951-62-1 313951-63-2

313951-64-3 313951-66-5 313951-68-7

313951-69-8 313951-70-1 313951-71-2

313951-72-3 313951-73-4 313951-74-5

313951-75-6

RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)

(**ghrelin** structure-function studies and minimal sequence

necessary for activation of growth hormone secretagogue receptor 1a)

REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 21 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:717906 HCAPLUS

DOCUMENT NUMBER: 133:329851

TITLE: **Ghrelin** Stimulates Gastric Acid Secretion and Motility in Rats

AUTHOR(S): Masuda, Yutaka; Tanaka, Tsuguhiko; Inomata, Norio; Ohnuma, Norio; Tanaka, Shoji; Itoh, Zen; Hosoda, Hiroshi; Kojima, Masayasu; Kangawa, Kenji

CORPORATE SOURCE: Suntory Institute for Medicinal Research & Development, Akaiwa, Chiyoda-machi, Ohra-gun, Gunma, 370-0503, Japan

SOURCE: Biochemical and Biophysical Research Communications (2000), 276(3), 905-908

CODEN: BBRCA9; ISSN: 0006-291X

PUBLISHER: Academic Press

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **Ghrelin**, a novel growth-hormone-releasing peptide, was discovered in rat and human stomach tissues. However, its physiol. and pharmacol. actions in the gastric function remain to be detd. Therefore, we studied the effects of rat **ghrelin** on gastric functions in urethane-anesthetized rats. The i.v. administrations of rat **ghrelin** at 0.8 to 20 .mu.g/kg dose-dependently increased not only gastric acid secretion measured by a lumen-perfused method, but also gastric motility measured by a miniature balloon method. The max. response in gastric acid secretion was almost equipotent to that of histamine (3 mg/kg, i.v.). Moreover, these actions were abolished by

pretreatment with either atropine (1 mg/kg, s.c.) or bilateral cervical vagotomy, but not by a histamine H2-receptor **antagonist** (famotidine, 1 mg/kg, s.c.). These results taken together suggest that **ghrelin** may play a physiol. role in the vagal control of gastric function in rats. (c) 2000 Academic Press.

IT 258338-12-4, Rat **ghrelin**

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(**ghrelin** stimulates gastric acid secretion and motility in rats)

REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 22 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:708572 HCAPLUS

DOCUMENT NUMBER: 135:29627

TITLE: Genomic organization of the human **GHRELIN** gene

AUTHOR(S): Wajnrajch, Michael P.; Ten, Irina S.; Gertner, Joseph M.; Leibel, Rudolph L.

CORPORATE SOURCE: Division of Pediatric Endocrinology, Weill Medical College of Cornell University, New York, NY, 10021, USA

SOURCE: Journal of Endocrine Genetics (2000), 1(4), 231-233
CODEN: JEJEF6; ISSN: 1565-012X

PUBLISHER: Freund

DOCUMENT TYPE: Journal

LANGUAGE: English

AB **GHRELIN**, the natural ligand for the growth hormone secretagogue receptor, was recently cloned. This "new" hormone is a short **octanoylated** peptide, produced in the stomach. We report the complete genomic organization of the human **GHRELIN** gene, its chromosomal location and vicinal polymorphic microsatellites. The gene is encoded by four exons spanning 4.3 kb of genomic DNA. **GHRELIN** is initially synthesized from four exons as a preprohormone, with a 23 amino acid signal sequence, and a 66 amino acid "tail". The mature **GHRELIN** gene product is encoded by exons one and two. The exons ranged from 20 to 117 bases while the introns spanned 194 to 2948 bases. The entire gene is found on a single BAC of approx. 105,000 bp and has been previously mapped to 3p26-25. The characterization of the gene's structure, its phys. location and the identification of vicinal polymorphic markers should provide useful reagents for the study of the mol. physiol. of growth.

IT 322637-19-4, **GHRELIN**, prepro

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence, mol. characterization, and processing of human **Ghrelin** prepro)

IT 213825-66-2 213825-69-5

RL: BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); PROC (Process)
(amino acid sequence; mol. characterization, and processing of human **Ghrelin** prepro)

IT 258279-04-8, **Ghrelin** (human)

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP (Properties); BIOL (Biological study); OCCU (Occurrence)
(amino acid sequence; of the mature form of human **Ghrelin**)

IT 288289-79-2, GenBank AF296558

RL: BOC (Biological occurrence); BSU (Biological study, unclassified); PRP

(Properties); BIOL (Biological study); OCCU (Occurrence)
(nucleotide sequence; DNA sequence, genomic organization, chromosome
localization and vicinal polymorphic markers including SNPs of the
human **GHRELIN** gene, encodes ligand for growth hormone
secretagogue receptor)

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS
RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 23 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:523259 HCAPLUS

DOCUMENT NUMBER: 133:329733

TITLE: Purification and characterization of rat des-Gln14-
ghrelin, a second endogenous ligand for the
growth hormone secretagogue receptor

AUTHOR(S): Hosoda, Hiroshi; Kojima, Masayasu; Matsuo, Hisayuki;
Kangawa, Kenji

CORPORATE SOURCE: Department of Biochemistry, National Cardiovascular
Center Research Institute, Suita, 565-8565, Japan

SOURCE: Journal of Biological Chemistry (2000), 275(29),
21995-22000

PUBLISHER: CODEN: JBCHA3; ISSN: 0021-9258

DOCUMENT TYPE: American Society for Biochemistry and Molecular
Biology

LANGUAGE: Journal

English

AB **Ghrelin**, a peptide purified from the stomach, is an endogenous
ligand for the growth hormone secretagogue receptor (GHS-R) and potentially
stimulates growth hormone release from the pituitary. **Ghrelin**
is modified with an n-octanoyl group at Ser3. This modification
is essential for the activity of **ghrelin**. Previously, it was
not known whether other ligands for GHS-R existed. Here, we report the
purification of the second endogenous ligand for GHS-R from rat stomach. This
ligand, named des-Gln14-**ghrelin**, is a 27-amino acid peptide,
whose sequence is identical to **ghrelin** except for one glutamine.
Southern blotting analysis under low hybridization conditions indicates that
no homolog for **ghrelin** exists in rat genomic DNA. Furthermore,
genomic sequencing and cDNA analysis indicate that des-Gln14-**ghrelin**
is not encoded by a gene distinct from **ghrelin** but is encoded by
an mRNA created by alternative splicing of the **ghrelin** gene.
This is the first example of a novel mechanism that produces peptide
multiplicity. Des-Gln14-**ghrelin** has an n-octanoyl
modification at Ser3 like **ghrelin**, which is also essential for
its activity. Des-Gln14-**ghrelin**-stimulated growth hormone
releases when injected into rats. Thus, growth hormone release is
regulated by two gastric peptides, **ghrelin** and des-Gln14-
ghrelin. ✓

IT 293339-41-0

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)

(amino acid sequence; rat des-Gln14-**ghrelin** sequence and
formation via splicing and growth hormone-secreting activity)

IT 293339-42-1

RL: PRP (Properties)

(amino acid sequence; rat des-Gln14-**ghrelin** sequence and
formation via splicing and growth hormone-secreting activity)

IT 287094-07-9, GenBank AB035699

RL: BSU (Biological study, unclassified); PRP (Properties); BIOL
(Biological study)

(nucleotide sequence; rat des-Gln14-**ghrelin** sequence and

formation via splicing and growth hormone-secreting activity)
IT 293735-04-3, Ghrelin [14-de-glutamine] (Rattus norvegicus)
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); MFM (Metabolic formation); PRP (Properties); BIOL (Biological study); FORM (Formation, nonpreparative)
(rat des-Gln14-ghrelin sequence and formation via splicing and growth hormone-secreting activity)
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 24 OF 26 HCAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2000:15363 HCAPLUS
DOCUMENT NUMBER: 132:74549
TITLE: Human signal peptide-containing proteins and their cDNA sequences
INVENTOR(S): Lal, Preeti; Tang, Y. Tom; Gorgone, Gina A.; Corley, Neil C.; Guegler, Karl J.; Baughn, Mariah R.; Akerblom, Ingrid E.; Au-Young, Janice; Yue, Henry; Patterson, Chandra; Reddy, Roopa; Hillman, Jennifer L.; Bandman, Olga
PATENT ASSIGNEE(S): Incyte Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 327 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2000000610 | A2 | 20000106 | WO 1999-US14484 | 19990625 |
| WO 2000000610 | A3 | 20000629 | | |
| W: | AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | |
| RW: | GH, GM, KE, LS, MW, SD, SL, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | |
| AU 9948349 | A1 | 20000117 | AU 1999-48349 | 19990625 |
| EP 1090118 | A2 | 20010411 | EP 1999-931942 | 19990625 |
| R: | BE, DE, ES, FR, GB, IT, NL | | | |
| JP 2002519030 | T2 | 20020702 | JP 2000-557363 | 19990625 |
| PRIORITY APPLN. INFO.: | | | US 1998-90762P | P 19980626 |
| | | | US 1998-94983P | P 19980731 |
| | | | US 1998-102686P | P 19981001 |
| | | | US 1998-112129P | P 19981211 |
| | | | US 1998-90762 | P 19980626 |
| | | | US 1998-94983 | P 19980731 |
| | | | US 1998-102686 | P 19981001 |
| | | | US 1998-112129 | P 19981211 |
| | | | WO 1999-US14484 | W 19990625 |

AB The invention provides 134 human signal peptide-contg. proteins (HSPP) and polynucleotides which identify and encode HSPP. Tissue-specific expression patterns are also provided. Biol. activity of HSPP-68 (potassium current using voltage clamp anal.) and HSPP-92 (protein

phosphatase measured by the hydrolysis of p-nitrophenyl phosphate) was demonstrated, and the HSPP proteins in general are expected to have useful activities. The invention also provides expression vectors, host cells, antibodies, agonists, and **antagonists**. The invention also provides methods for diagnosing, treating, or preventing disorders assocd. with expression of HSPP.

IT 213825-66-2P

RL: ANT (Analyte); BOC (Biological occurrence); BPN (Biosynthetic preparation); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); OCCU (Occurrence); PREP (Preparation); USES (Uses)
(amino acid sequence; human signal peptide-contg. proteins and their cDNA sequences)

L10 ANSWER 25 OF 26 HCAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2000:3661 HCAPLUS

DOCUMENT NUMBER: 132:146745

TITLE: **Ghrelin** is a growth-hormone-releasing acylated peptide from stomach

AUTHOR(S): Kojima, Masayasu; Hosoda, Hiroshi; Date, Yukari;

CORPORATE SOURCE: Nakazato, Masamitsu; Matsuo, Hlsayuki; Kangawa, Kenjli
Department of Biochemistry, National Cardiovascular Center Research Institute, Fujishirodai, Suita, Osaka, 565-8565, Japan

SOURCE: Nature (London) (1999), 402(6762), 656-660

CODEN: NATUAS; ISSN: 0028-0836

PUBLISHER: Macmillan Magazines

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Small synthetic mols. called growth-hormone secretagogues (GHSs) stimulate the release of growth hormone (GH) from the pituitary. They act through GHS-R, a G-protein-coupled receptor for which the ligand is unknown. Recent cloning of GHS-R strongly suggests that an endogenous ligand for the receptor does exist and that there is a mechanism for regulating GH release that is distinct from its regulation by hypothalamic growth-hormone-releasing hormone (GHRH). We now report the purifn. and identification in rat stomach of an endogenous ligand specific for GHS-R. The purified ligand is a peptide of 28 amino acids, in which the serine 3 residue is **n-octanoylated**. The acylated peptide specifically releases GH both in vivo and in vitro, and **O-n-octanoylation** at serine 3 is essential for the activity. We designate the GH-releasing peptide '**ghrelin**' (ghre is the Proto-Indo-European root of the word 'grow'). Human **ghrelin** is homologous to rat **ghrelin** apart from two amino acids. The occurrence of **ghrelin** in both rat and human indicates that GH release from the pituitary may be regulated not only by hypothalamic GHRH, but also by **ghrelin**. xDS

IT 213825-69-5 258259-90-4

RL: PRP (Properties)

(amino acid sequence; rat and human **ghrelin** sequence and growth-hormone-releasing activity after isolation from stomach)

IT 213825-66-2P 258259-89-1P

RL: PRP (Properties); PUR (Purification or recovery); PREP (Preparation)

(amino acid sequence; rat and human **ghrelin** sequence and growth-hormone-releasing activity after isolation from stomach)

IT 252925-13-6, GenBank AB029433 252925-14-7, GenBank

AB029434

RL: PRP (Properties)

(nucleotide sequence; rat and human **ghrelin** sequence and

growth-hormone-releasing activity after isolation from stomach)
 IT 258279-04-8P, Ghrelin (human) 258338-12-4P,
 Ghrelin (Rattus norvegicus)
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); PUR (Purification or recovery); BIOL (Biological study); PREP (Preparation)
 (rat and human ghrelin sequence and growth-hormone-releasing activity after isolation from stomach)
 REFERENCE COUNT: 27 THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 26 OF 26 HCAPLUS COPYRIGHT 2003 ACS
 ACCESSION NUMBER: 1998:672664 HCAPLUS
 DOCUMENT NUMBER: 129:271092
 TITLE: Cloning and cDNA sequence of a human motilin homolog and its role in gastric motility
 INVENTOR(S): Sheppard, Paul O.; Deisher, Theresa A.
 PATENT ASSIGNEE(S): Zymogenetics, Inc., USA
 SOURCE: PCT Int. Appl., 69 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|-------------|
| WO 9842840 | A1 | 19981001 | WO 1998-US5620 | 19980323 |
| W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM | | | | |
| RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG | | | | |
| US 6380158 | B1 | 20020430 | US 1997-822897 | 19970324 |
| AU 9865769 | A1 | 19981020 | AU 1998-65769 | 19980323 |
| AU 726423 | B2 | 20001109 | | |
| EP 975760 | A1 | 20000202 | EP 1998-911928 | 19980323 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI | | | | |
| BR 9808059 | A | 20000308 | BR 1998-8059 | 19980323 |
| JP 2001513651 | T2 | 20010904 | JP 1998-543276 | 19980323 |
| US 6291653 | B1 | 20010918 | US 1998-46479 | 19980323 |
| NO 9904614 | A | 19991123 | NO 1999-4614 | 19990923 |
| MX 9908778 | A | 20000228 | MX 1999-8778 | 19990924 |
| US 2001041791 | A1 | 20011115 | US 2001-794987 | 20010227 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1997-41102P | P 19970324 |
| | | | US 1997-822897 | A 19970324 |
| | | | US 1998-46479 | A3 19980323 |
| | | | WO 1998-US5620 | W 19980323 |

AB The present invention is directed to polynucleotides, polypeptides and peptide fragments thereof, and uses thereof for a novel human fetal pancreatic cDNA sequence, designated zsig33, which has homol. to motilin. Zsig33 is secreted as mature peptide comprising residues 24-41 of the prepro, 117-residue precursor. Tissue distribution of the mRNA for the novel polypeptide is specific to the stomach, small intestine and pancreas. The zsig33 gene was mapped to chromosome 3p26.1. The present

invention further includes agonists, antagonists, antibodies, host cells expressing the cDNA encoding the novel motilin homologs and methods for increasing gastric motility using the novel mols.

IT 213815-73-7P, 1-14-Gastrointestinal hormone zsig33 (human)

213815-74-8P, Gastrointestinal hormone zsig33 (human)

213825-66-2P 213825-69-5P 213828-15-0P

RL: BPN (Biosynthetic preparation); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(amino acid sequence; cloning and cDNA sequence of a human motilin homolog and its role in gastric motility)

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

=> select hit rn 110 1-26

E1 THROUGH E118 ASSIGNED

=> fil reg

FILE 'REGISTRY' ENTERED AT 16:09:14 ON 17 JAN 2003

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 16 JAN 2003 HIGHEST RN 479347-08-5

DICTIONARY FILE UPDATES: 16 JAN 2003 HIGHEST RN 479347-08-5

TSCA INFORMATION NOW CURRENT THROUGH MAY 20, 2002

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. See HELP PROPERTIES for more information. See STNote 27, Searching Properties in the CAS Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> s e1-e118 and 11

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90 95 102

L11 ANSWER 1 OF 102 REGISTRY COPYRIGHT 2003 ACS
RN 475223-96-2 REGISTRY
CN Ghrelin, prepro- (human) (9CI) (CA INDEX NAME)
OTHER NAMES:
CN 7: PN: WO02090387 FIG: 1 claimed protein
LC STN Files: CA, CAPLUS, TOXCENTER
SQL 117
RN 475223-96-2 REGISTRY

SEQ 1 MPSPGTVCSL LLLGMLWLDL AMAGSSFLSP EHQRVQQRKE SKKPPAKLQP

HITS AT: 24-27

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RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 137:367967

L11 ANSWER 5 OF 102 REGISTRY COPYRIGHT 2003 ACS

RN 374629-83-1 REGISTRY

CN L-Lysine, glycyl-L-seryl-O-(1-oxooctyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutaminyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS

NTE modified

| type | location | description |
|--------------|----------|-----------------|
| modification | Ser-3 - | 1-oxooctyl<Oct> |

SQL 11

RN 374629-83-1 REGISTRY

SEQ 1 GSSFLSPEHQ K

====

HITS AT: 1-4

REFERENCE 1: 135:366876

L11 ANSWER 10 OF 102 REGISTRY COPYRIGHT 2003 ACS

RN 342047-04-5 REGISTRY

CN L-Glutamine, N-acetylglycyl-L-seryl-O-(1-oxooctyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS

NTE modified

| type | location | description |
|---------------|----------|-----------------|
| terminal mod. | Gly-1 - | N-acetyl |
| modification | Ser-3 - | 1-oxooctyl<Oct> |

SQL 10

RN 342047-04-5 REGISTRY

SEQ 1 GSSFLSPEHQ

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HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:366876

REFERENCE 2: 135:602

L11 ANSWER 15 OF 102 REGISTRY COPYRIGHT 2003 ACS

RN 342046-95-1 REGISTRY

CN L-Arginine, glycyl-L-seryl-O-(1-oxooctyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutaminyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS
NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|-----------------|
| modification | Ser-3 | 1-oxooctyl<Oct> |

SQL 11

RN 342046-95-1 REGISTRY

SEQ 1 GSSFLSPEHQ R

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:602

L11 ANSWER 20 OF 102 REGISTRY COPYRIGHT 2003 ACS

RN 342046-88-2 REGISTRY

CN L-Arginine, glycyl-L-seryl-O-(1-oxohexyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutaminyl-L-lysyl-L-alanyl-L-glutaminyl-L-glutaminyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS

NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|-----------------|
| modification | Ser-3 | 1-oxohexyl<Hex> |

SQL 28

RN 342046-88-2 REGISTRY

SEQ 1 GSSFLSPEHQ KAQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:366876

REFERENCE 2: 135:602

L11 ANSWER 25 OF 102 REGISTRY COPYRIGHT 2003 ACS

RN 322483-17-0 REGISTRY

CN Ghrelin (Anguilla japonica prepro) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 32: PN: WO0107475 SEQID: 32 claimed protein

LC STN Files: CA, CAPLUS

SQL 108

RN 322483-17-0 REGISTRY

SEQ 1 MKRTAYIILL VCVLALWMDS VQAGSSFLSP SQRPGKDKK PPRVGRDSD

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HITS AT: 24-27

REFERENCE 1: 134:142304

L11 ANSWER 30 OF 102 REGISTRY COPYRIGHT 2003 ACS

RN 321975-37-5 REGISTRY

CN L-Arginine, glycyl-L-seryl-O-(phenylmethyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutamyl-L-arginyl-L-valyl-L-glutamyl-L-glutamyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutamyl-L-prolyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS

NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|-------------------|
| modification | Ser-3 | phenylmethyl<Bzl> |

SQL 28

RN 321975-37-5 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 134:142304

L11 ANSWER 35 OF 102 REGISTRY COPYRIGHT 2003 ACS

RN 321975-27-3 REGISTRY

CN L-Arginine, glycyl-L-seryl-O-octyl-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutamyl-L-arginyl-L-valyl-L-glutamyl-L-glutamyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutamyl-L-prolyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS

NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|---------------------------|
| modification | Ser-3 | undetermined modification |

SQL 28

RN 321975-27-3 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:366876

REFERENCE 2: 135:602

REFERENCE 3: 134:142304

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RN 321974-99-6 REGISTRY

CN L-Lysinamide, glycyl-L-seryl-O-(1-oxooctyl)-L-seryl-D-phenylalanyl- (9CI) (CA INDEX NAME)

LC STN Files: CA, CAPLUS
NTE modified

| type | location | description |
|---------------|----------|------------------|
| terminal mod. | Lys-5 | C-terminal amide |
| modification | Ser-3 | 1-oxooctyl<Oct> |

SQL 5
RN 321974-99-6 REGISTRY

SEQ 1 GSSFK

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 134:142304

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RN 321974-88-3 REGISTRY
CN L-Leucine, glycyl-L-seryl-O-(1-oxooctyl)-L-seryl-L-phenylalanyl- (9CI)
(CA INDEX NAME)
LC STN Files: CA, CAPLUS
NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|-----------------|
| modification | Ser-3 | 1-oxooctyl<Oct> |

SQL 5
RN 321974-88-3 REGISTRY

SEQ 1 GSSFL

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:175617

REFERENCE 2: 135:602

REFERENCE 3: 134:142304

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RN 321974-78-1 REGISTRY
CN L-Arginine, glycyl-L-seryl-O-(1-oxo-3-phenylpropyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutaminyl-L-arginyl-L-valyl-L-glutaminyl-L-glutaminyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)
LC STN Files: CA, CAPLUS
NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|----------------------|
| modification | Ser-3 | 1-oxo-3-phenylpropyl |

SQL 28
RN 321974-78-1 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQRKESKK PPAKLQPR
=====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:366876

REFERENCE 2: 135:602

REFERENCE 3: 134:142304

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RN 321974-68-9 REGISTRY
CN L-Histidinamide, glycyl-L-seryl-O-(1-oxooctyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl- (9CI) (CA INDEX NAME)
LC STN Files: CA, CAPLUS
NTE modified

| type | location | description |
|---------------|----------|------------------|
| terminal mod. | His-9 | C-terminal amide |
| modification | Ser-3 | 1-oxooctyl<Oct> |

SQL 9
RN 321974-68-9 REGISTRY

SEQ 1 GSSFLSPEH
=====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 135:175617

REFERENCE 2: 135:602

REFERENCE 3: 134:142304

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RN 321974-54-3 REGISTRY
CN L-Arginine, glycyl-L-seryl-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-threonyl-L-tyrosyl-L-lysyl-L-asparaginyll-L-isoleucyl-L-glutaminyll-L-glutaminyll-L-glutaminyll-L-lysylglycyl-L-threonyl-L-arginyl-L-lysyl-L-prolyl-L-threonyl-L-alanyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 25: PN: WO0107475 SEQID: 25 claimed protein

LC STN Files: CA, CAPLUS

SQL 24

RN 321974-54-3 REGISTRY

SEQ 1 GSSFLSPTYK NIQQQKGTRK PTAR
=====

HITS AT: 1-4

REFERENCE 1: 134:142304

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RN 321974-44-1 REGISTRY

CN L-Arginine, glycyl-L-seryl-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutaminyl-L-lysyl-L-alanyl-L-glutaminyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutaminyl-L-prolyl- (9CI)
(CA INDEX NAME)

OTHER NAMES:

CN 10: PN: WO0107475 SEQID: 10 claimed protein

LC STN Files: CA, CAPLUS

SQL 27

RN 321974-44-1 REGISTRY

SEQ 1 GSSFLSPEHQ KAQRKESKKP PAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 134:142304

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RN 313951-75-6 REGISTRY

CN L-Phenylalaninamide, glycyl-L-seryl-O-(1-oxooctyl)-L-seryl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN EP 01037 - NOT EP 01037!

LC STN Files: CA, CAPLUS

NTE modified

| type | ----- | location | ----- | description |
|---------------|-------|----------|-------|------------------|
| terminal mod. | Phe-4 | - | | C-terminal amide |
| modification | Ser-3 | - | | 1-oxooctyl<Oct> |

SQL 4

RN 313951-75-6 REGISTRY

SEQ 1 GSSF

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 137:73541

REFERENCE 2: 136:32165

REFERENCE 3: 135:175617

REFERENCE 4: 135:602

REFERENCE 5: 134:142304

REFERENCE 6: 134:51509

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RN 313951-70-1 REGISTRY

SEE L10 #20/26
too new
published 10/2000

*

CN L-Arginine, glycyl-L-seryl-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutamyl-L-arginyl-L-valyl-L-glutamyl-L-glutamyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-O-(1-oxooctyl)-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutamyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 22: PN: WO0192292 SEQID: 21 claimed protein

LC STN Files: CA, CAPLUS

NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|-----------------|
| modification | Ser-18 | 1-oxooctyl<Oct> |

SQL 28

RN 313951-70-1 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 136:32165

REFERENCE 2: 134:51509

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RN 313951-63-2 REGISTRY

CN L-Arginine, glycyl-L-seryl-O-(tricyclo[3.3.1.1^{3,7}]dec-1-ylacetyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutamyl-L-arginyl-L-valyl-L-glutamyl-L-glutamyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutamyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 17: PN: WO0192292 SEQID: 16 claimed protein

LC STN Files: CA, CAPLUS

NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|---------------------------|
| modification | Ser-3 | undetermined modification |

SQL 28

RN 313951-63-2 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 136:32165

REFERENCE 2: 134:51509

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RN 313951-58-5 REGISTRY

CN L-Arginine, glycyl-L-seryl-O-acetyl-L-seryl-L-phenylalanyl-L-leucyl-L-

seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutaminyl-L-arginyl-L-valyl-L-glutaminyl-L-glutaminyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 12: PN: WO0192292 SEQID: 11 claimed protein

LC STN Files: CA, CAPLUS

NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|-------------|
| modification | Ser-3 | acetyl<Ac> |

SQL 28

RN 313951-58-5 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 136:32165

REFERENCE 2: 134:51509

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RN 307950-60-3 REGISTRY

CN L-Arginine, glycyl-L-seryl-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutaminyl-L-lysyl-L-alanyl-L-glutaminyl-L-glutaminyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutaminyl-L-prolyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2: PN: WO0107475 SEQID: 2 claimed protein

LC STN Files: CA, CAPLUS

SQL 28

RN 307950-60-3 REGISTRY

SEQ 1 GSSFLSPEHQ KAQQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 137:304938

REFERENCE 2: 135:366876

REFERENCE 3: 134:142304

REFERENCE 4: 134:740

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RN 258279-04-8 REGISTRY

CN Ghrelin (human) (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 2: PN: WO0192292 SEQID: 1 claimed protein

CN Ghrelin (human clone CTB-187P1 gene GHRELIN))

CN Human ghrelin
CN L-Arginine, glycyl-L-seryl-O-(1-oxooctyl)-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutamyl-L-arginyl-L-valyl-L-glutamyl-L-glutamyl-L-arginyl-L-lysyl-L-.alpha.-glutamyl-L-seryl-L-lysyl-L-lysyl-L-prolyl-L-prolyl-L-alanyl-L-lysyl-L-leucyl-L-glutamyl-L-prolyl-
LC STN Files: BIOTECHNO, CA, CAPLUS, CHEMCATS, EMBASE, TOXCENTER
NTE modified (modifications unspecified)

| type | location | description |
|--------------|----------|-----------------|
| modification | Ser-3 | 1-oxooctyl<Oct> |

SQL 28

RN 258279-04-8 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQRKESKK PPAKLQPR

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

REFERENCE 1: 138:22305

REFERENCE 2: 137:346579

REFERENCE 3: 137:304938

REFERENCE 4: 137:195843

REFERENCE 5: 137:135310

REFERENCE 6: 137:73541

REFERENCE 7: 136:260242

REFERENCE 8: 136:241940

REFERENCE 9: 136:145365

REFERENCE 10: 136:129319

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RN 213815-73-7 REGISTRY

CN L-Glutamine, glycyl-L-seryl-L-seryl-L-phenylalanyl-L-leucyl-L-seryl-L-prolyl-L-.alpha.-glutamyl-L-histidyl-L-glutamyl-L-arginyl-L-valyl-L-glutamyl- (9CI) (CA INDEX NAME)

OTHER NAMES:

CN 1-14-Gastrointestinal hormone zsig33 (human)

CN 17: PN: WO0138355 SEQID: 2 claimed sequence

LC STN Files: CA, CAPLUS, USPATFULL

SQL 14

RN 213815-73-7 REGISTRY

SEQ 1 GSSFLSPEHQ RVQQ

====

HITS AT: 1-4

RELATED SEQUENCES AVAILABLE WITH SEQLINK

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REFERENCE 1: 135:14332

REFERENCE 2: 129:271092

Searched by M. Smith